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A PREDICTIVE STUDY OF THE INCIDENCE OF VOMITING IN IRRADIATED M--ETC(U)
OCT 79 G A GRANT, A B CAIRNIE, R K HARDING

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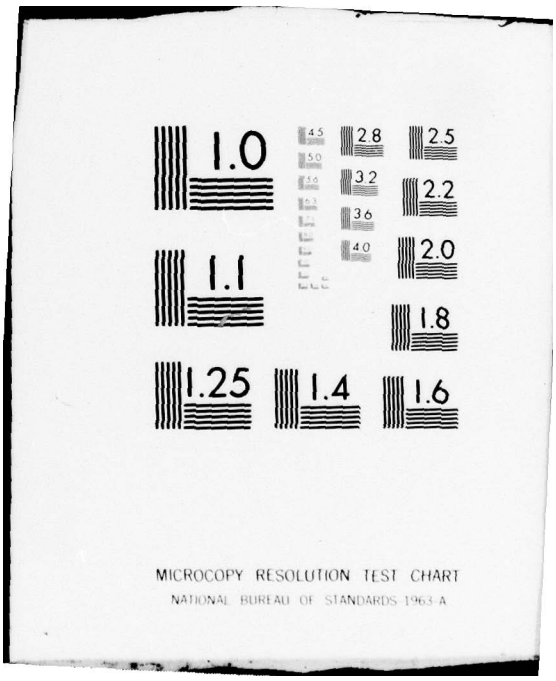
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DEFENCE RESEARCH ESTABLISHMENT OTTAWA

DREO REPORT NO. 817
DREO R 817

A PREDICTIVE STUDY OF THE INCIDENCE OF VOMITING IN IRRADIATED MILITARY PERSONNEL

by
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N.T. Gridgeman and W.D. Rider

OCTOBER 1979
OTTAWA

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DEPARTMENT OF NATIONAL DEFENCE
CANADA

DEFENCE RESEARCH ESTABLISHMENT OTTAWA

(14) DREO-R-
REPORT NO. 817

(9) Project rept. 1974—1978,

(6) A PREDICTIVE STUDY OF THE INCIDENCE OF VOMITING IN IRRADIATED MILITARY PERSONNEL.

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(12) 39

(11) OCTOBER 1979
OTTAWA

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ABSTRACT

The scientific literature on the incidence in man of vomiting and other prodromal effects of ionising radiation is analysed and related to the guidance given in STANAG 2866. New data obtained from observations of 271 patients who received 600 to 1000 rad to either the upper or lower half of the body are analysed. The incidence of vomiting was 81 per cent in those who received radiation to the upper half of the body and 44 per cent for the lower half. The time to the first and last vomiting episodes for upper-body radiation were on average about 60 and 150 min from the start of the irradiation. The average number of episodes was 4.5; the average duration of an episode just over 2 min. None of these parameters changed appreciably with the doses used. Predictions are made of the time required for various percentages of military personnel to start, and then to finish, vomiting after being exposed to radiation.

RÉSUMÉ

La littérature scientifique sur la fréquence chez l'homme de vomissement et d'autres effets prodromaux dûs à la radiation ionisante est analysée et rattachée aux directives données dans STANAG 2866. Les nouvelles données obtenues d'après les observations chez 271 patients qui ont reçu de 600 à 1000 rad, soit à la partie supérieure, soit à la partie inférieure du corps, sont analysées. La fréquence de vomissement était de 81% chez ceux qui avaient reçu la radiation sur la partie supérieure du corps, et de 44% pour la partie inférieure du corps. Le premier épisode de vomissement dans les cas de radiation à la partie supérieure du corps se produisait environ 60 minutes après le début de l'irradiation, et le dernier épisode, environ 150 minutes après. Le nombre moyen d'épisodes était 4.5, avec une durée moyenne pour chaque épisode d'un peu plus de 2 minutes. Aucun des paramètres n'avait changé considérablement avec les doses utilisées. Des prédictions sont faites afin d'établir le temps requis par les divers pourcentages du personnel militaire pour commencer et ensuite terminer de vomir après l'exposition à la radiation.

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INTRODUCTION

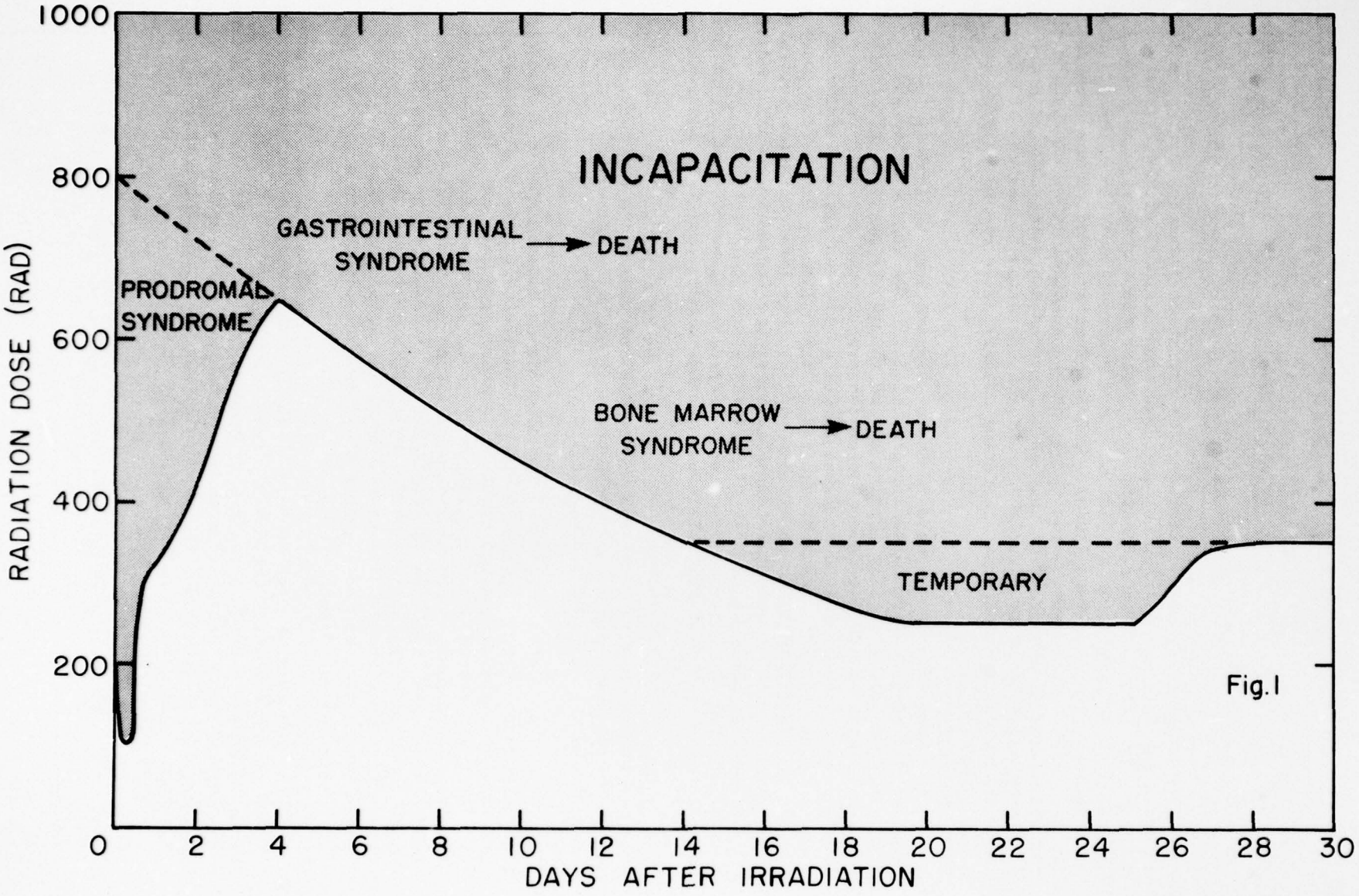
This study of the incidence of radiation-induced vomiting (emesis) in human subjects was carried out on irradiated patients at the Princess Margaret Hospital, Toronto, Canada. The observations were made on patients who received the radiation as part of their treatment for the alleviation of pain (Fitzpatrick and Rider, 1976). The information obtained has been used for two research purposes: first, study of the possibility of mitigation of the unpleasant side-effects of the radiation treatments for cancer; and second, prediction of the likelihood of incapacitation of members of the armed forces exposed to radiation during combat. This second purpose is dealt with here.

A healthy man exposed to acute, penetrating, whole-body radiation acquires a dose-dependent mortality probability. The dose causing 50% mortality (LD-50) is usually said to be 300 to 350 rad whole-body, although figures as high as 450 have been quoted (absorbed dose, measured at the mid-line). The corresponding LD-95 level is put at 150 rad higher (and, symmetrically, the LD-5 level at 150 rad lower). Time to death from doses of 600 rad is usually taken to be at least 6 days, but incapacitation would occur earlier. It is expected that members of the forces in combat receiving 600 rad or less would be capable of performing some duties before hospitalization would become necessary. For doses above 600 rad one should not rely on performance, but this would depend to some extent on motivation.

The estimated time to incapacitation is shown in Fig. 1, which is based on STANAG 2866 (2). It must be emphasized that there are few data on which to base these estimates, and perhaps it would be better to refer to "conventional wisdom" rather than objective analysis.

Fig. 1 also indicates that there is an expectation of a prodromal incapacitation during the first two days, attributable mainly to vomiting, but also to anorexia (loss of appetite), nausea, and fatigue. This is not the "early transient incapacitation" said to be experienced within minutes of a very large dose. Prodromal incapacitation is of military importance because it occurs even with sublethal doses. It takes place during the first two days, starting within an hour or two. This period may be vital for the successful completion of a mission. Emesis would be particularly incapacitating for men wearing face masks (either for oxygen administration or for chemical/biological protection).

These early effects - anorexia, nausea, vomiting, and fatigue - can be used as general indications that irradiation has occurred, but they are not to be recommended as a basis for prognosis. They are transient, lasting a few days at most. With large doses the subject will experience somewhat later a second set of symptoms, especially diarrhoea, which supervenes without any symptom-free interval (Fig. 1).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RADIATION DOSE (RAD)
DAYS AFTER IRRADIATION
INCAPACITATION
GASTROINTESTINAL SYNDROME
DEATH
PRODROMAL SYNDROME
BONE MARROW SYNDROME
DEATH
TEMPORARY

Fig.1

Fig. 1. The predictions of STANAG 2866, which gives the expected response of military personnel exposed to whole-body radiation, are depicted in Figure 1. The ordinate is the radiation dose received, and the abscissa the days to incapacitation. Prodromal incapacitation occurs early and is transient; with low doses it may be the only manifestation. With doses above 700 rad the prodromal syndrome is followed directly by the gastrointestinal syndrome, but with lower doses there is a transient recovery. The LD-50 is 300 to 350 rad. Persons receiving 250 to 350 rad will require hospitalisation for a period from 3 to 4 weeks after irradiation but most will recover spontaneously if given adequate medical attention. Recovery from doses much above 300 rad would require sophisticated medical intervention of a kind not likely to be available to large numbers of battlefield casualties.

In this report we shall review the state of knowledge of the dependence of prodromal incapacitation on such factors as dose and site (i.e., the part of the body receiving the radiation), and present new data on the onset and the duration of vomiting (this being the most incapacitating feature of the prodromal phenomenon). In our study we have paid particular attention to the time parameters of each vomiting episode because of the military significance of temporary incapacitation of personnel performing essential duties.

PREVIOUS STUDIES

The symptoms experienced by those irradiated at Hiroshima and Nagasaki included anorexia, nausea, vomiting and fatigue during the first few days (Ohkita, 1975). The observations are of limited usefulness in predicting effects on combat troops because of the high incidence at that time of malnutrition and disease in the Japanese population which caused similar symptoms, because of the absence of information on radiation doses received, and because of the haphazard nature of the observations due to the chaos in those cities just after the bombs fell.

More detailed information has been collected in several studies on patients who received radiation as part of their treatment. One group, studied by Court Brown and co-workers between 1953 and 1955, consisted largely of patients who received radiation doses to the spine and sacro-iliac joints for ankylosing spondylitis. They described the effects as follows (Court Brown and Mahler, 1953):

> *The pattern of events following such a dose of X-rays was found to consist of, firstly, a latent period before any symptoms commenced, secondly a period of acute disturbance, and finally a period of recovery. The mean length of the latent period, considering the whole group of patients, was nearly two and three-quarter hours. When a comparison was made between those patients who were most severely upset and who vomited, and those who were less upset and did not vomit, the mean length of the latent period was found to be shorter in the first group than in the second group, the difference being approximately three-quarters of an hour.*
>
> *The latent period terminates with the sudden onset of symptoms, the outstanding complaints at this time being fatigue, anorexia and nausea, and these remain present for at least an hour before subsiding, in those patients who are only mildly upset. Where the period of acute disturbance is more severe, after about an hour the fatigue and nausea become accentuated, and in some instances vomiting and retching supervene. One bout of vomiting may occur, or vomiting may occur at intervals of two to three hours in the most severely upset patients before the recovery period ensues.*

Dependent on the degree of upset in the period of acute disturbance, the recovery phase may last less than one day or for as long as five days. During this phase there is a gradual disappearance of firstly nausea, then fatigue and finally anorexia.

Objective assessment of such symptoms as fatigue, anorexia and nausea is practically impossible but we have a very strong subjective impression that the fatigue experienced is in some way dissociated from the nausea and anorexia. Thus in some patients fatigue has been undoubtedly the only symptom, whilst in others it is certainly the predominant symptom, nausea and anorexia being only fleeting complaints and vomiting not occurring at all. At the other end of the scale, a group of patients has been collected in whom nausea and repeated vomiting were the only complaints. It was also remarkable in these latter patients that, almost immediately after vomiting had ceased, the patients were symptom-free. It appears also from studies which have been carried out into electrolyte excretion that certain changes are related to the symptom of fatigue and are absent when fatigue is absent, even though nausea and vomiting occur. These impressions suggest that two disorders underlie these symptoms, one associated with fatigue and the other with nausea and vomiting.

34 of the 50 patients observed were also subjected to sham irradiations to control the possible effects of emotional and psychological disturbances in producing symptoms. 8 of these patients developed symptoms, as opposed to 46 out of the 50 exposed to the actual irradiation, and in all instances the symptoms lacked the characteristic pattern and timing of those following the real irradiation.

These studies also are deficient for the present purpose because of the limited information on dosimetry and the restriction of the radiation to certain regions of the body.

Miller, Fletcher and Gerstner (1958) reported on the effects of whole-body radiation given to cancer patients. As the study progressed they gradually increased the dose they were prepared to give patients to 200 r (mid-line dose free-in-air, average absorbed dose 130 rad) given at 3.8 r/min. Of the 30 patients who received 200 r, 27 reported experiencing within a few hours fatigue, decreased energy, drowsiness, or malaise accompanied by anorexia; 24 reported nausea within 72 hours; and 17 vomited. Only 2 became non-ambulatory and received parenteral fluid replacement. They stress that these patients might be expected to experience some nausea and vomiting because of their disease state quite apart from the radiation. The effects found in patients receiving lower doses are shown in the following table and give some indication of a possible threshold at about 125 r (80 rad).

Dose(r)	No. of Patients	Nausea	Vomiting
15-75	199	1/199	none
100	18	none	none
125-175	11	?	7/11
200	30	24/30	17/30

The final point is that the effects were first noted at about 2 hours after irradiation and lasted for 1 day.

Court Brown and Abbatt (1954) found that the latent period was somewhat shorter in patients with a high surface dose to surface area ratio, but this appears to be linked to the physician's choice of dose for patients of various sizes. Gerstner (1960) paid close attention to the length of the latent period in his study and concluded it was not influenced much by size of the field or the dose, within certain limits. The median latent period was 3 hours with a range of 1 to 4½ hours and the variation was attributed largely to variation in individual susceptibility.

A larger study of whole-body-irradiated patients was made by Lushbaugh and colleagues (Lushbaugh, Comas and Hofstra, 1967; Langham, 1967; and Lushbaugh, Comas, Edwards and Andrews, 1968). The final report included 504 subjects for whom adequate dose measurements were made. The estimates of the doses to a 26-cm-diameter sphere of tissue in the epigastric region required to cause 50 per cent of patients to show various clinical responses were:

	ED-50	
Clinical Response	Normal Arithmetic Distribution	Log-Normal Distribution
	(rad)	(rad)
Anorexia (within 2 days)	121±19	97×÷1.12
Nausea (within 2 days)	172±17	139×÷1.14
Fatigue (within 6 weeks)	181±25	147×÷1.24
Vomiting (within 2 days)	214±22	183×÷1.21
Diarrhoea (within 6 weeks)	239±32	230×÷2.02
Death (within 60 days)	251±28	235×÷1.32

Attempts to estimate the slopes of the probit regression lines on dose were not very successful because of limited data and the findings are more reliable when the data is used to estimate just the ED-50's shown above. There is no basis in this study for discriminating between the normal and log-normal distributions and each can be pushed to patently wrong conclusions; fortunately if one focuses on the 50 per cent response level there is good agreement and a choice can be avoided.

Lushbaugh and his co-workers used a computer programmed to determine whether or not a patient displayed a set of clinical symptoms which had been defined as fatigue etc., and after their first report (Lushbaugh et al., 1967) they gave only ED-50 and regression equations of probit of response on dose or log-dose. However in their first report, with 100 subjects, they gave the group means used to calculate the regression equations. After a mean dose of 31.7 rad 2/30 vomited, after 65.2 rad 8/38 vomited, etc. Lushbaugh et al. then "corrected" the response for intercurrent vomiting due to non-radiation factors before calculating their regression equations. The statistical procedures are correct, but the validity of the prediction of radiation effects on combat forces is very questionable. Sophisticated manipulation of limited data derived from cancer patients on the point of death caused by their disease may lead to false conclusions.

The NAS-NRC study (Langham, 1967), which was based on Lushbaugh's extended data, estimated that reducing the dose rate to low levels would increase the ED-50 for prodromal effects by a factor of 2.5. Lushbaugh et al. (1968) found that none of 9 patients who received 100 to 200 r at 1.5 r/h for 20 hours/day had gastrointestinal responses, but it is believed that this investigation ceased abruptly when subsequent experience showed that low dose-rate did not mitigate significantly the prodromal effects.

In contrast to the reports already cited, Rider and Hasselback (1968) studied a group of 20 young patients with Ewing's tumour of bone who were "all in good general condition and had normal peripheral blood pictures and bone marrows .... these individuals were as close to normal as one can justifiably irradiate". The absorbed dose was 300 rad given uniformly to the whole body. Following an asymptomatic interval of 45 to 60 min a 15-min episode of projectile vomiting started. Periods of vomiting alternated with sleep and fatigue for about 6 hours. The patients were discharged next day and were symptomatically well until they encountered a bone-marrow depression at about 25 days which required barrier nursing to prevent infection.

The study to be reported suffers from the defects outlined earlier which are shared by all studies utilising cancer patients. Nevertheless the new information on the time- and dose-dependence of vomiting, also the sensitivity of various regions of the body, will be important in military planning.

PRESENT STUDY

The occurrence of vomiting was followed in a group of patients who had been selected by their physicians to receive doses of γ radiation for alleviation of pain due to disseminated secondary tumours, mainly in bone. All patients so treated at the Princess Margaret Hospital from April 1974 to April 1978 who gave their permission were included in this study. The γ radiation was given either to the upper or lower half of the body, depending on the site of greatest pain (Fitzpatrick and Rider, 1976). (The

two halves of the body are defined with reference to the umbilicus.) No measure of physical fitness was applied, but it is obvious that this group is not representative of soldiers. However, they were typically not confined to bed at the time of treatment. Some patients returned after a period of about 6 weeks for necessary radiation treatment to the other half of the body. Because of this complication we shall henceforward distinguish between subjects (i.e., patients) and cases (i.e., individual irradiations and their consequences). There were 271 subjects, of whom 41 were "repeaters" (treatment of the other half of the body), so that the number of cases was 312. The essential information as regards age and sex in the group is given in Table I.

The doses received depended on the needs of the patients and were within the range of 100 to 1000 rad. However there were three concentration points: 600, 800, and 1000 rad, and it seemed best to trichotomize the cases accordingly. Specifically, the subgroups are, in terms of dosage: (i) 600 or less, (ii) about 800 (the biggest group), and (iii) 1000 or more. A statistical probe indicated that no extra information would emerge from finer subgroupings. The sizes of these subgroups, and how they break down further in terms of sex, site and dose, are given in Tables II and III.

The absorbed dose was calculated for the midplane of the trunk of the body and bolus was used as necessary to compensate for differences in body depth along its length. The dose rate free-in-air was usually about 45 rad/min, but a few irradiations were carried out at high dose rate on a linear accelerator. The patient received half the dose supine from an overhead Co^{60} source pointing vertically downward, and was then turned to receive the second half prone. The average duration of the irradiation was about 30 min, including the break to turn the patient and make necessary adjustments. The patient was advised of the probability of vomiting (and of the observational study). After irradiation he passed into the care of a nurse who gave him a basin and accompanied him to the recovery room where he rested in bed for up to 6 hours, by which time the vomiting had normally ceased, but the patient could elect to return to the ward earlier. In that event the special nurse was no longer assigned to observe him; however, an effort was made to transfer any notes from the ward records to the data sheets supplied for analysis. It was the consensus that vomiting after leaving the recovery room was a rare event. Patients were usually held in hospital one night and discharged the following day.

The data sheets used for recording the data are shown in Appendix 1. Continuation sheets were available. The nurse received no instructions other than those on the sheets. When the analysis started it became clear that nausea was very frequently recorded by the nurse when the patient vomited, and was not often recorded independently; for this reason the nausea incidence was not analysed. Although degrees of vomiting, determined by the volume of vomitus, were recorded, this differentiation was ignored in the analysis because all degrees were judged to be equally incapacitating.

The information on the data sheets was coded and punched on computer cards following the procedure given in Appendix 1.

TABLE I

Age Distribution of the 271 Subjects

Number of Subjects by Sex			Age Characteristics (years)		
			Average	Range	"75% brackets"[b]
M	118 singles 24 repeaters[a]	142	62	16 to 84	51 to 73
F	112 singles 17 repeaters	129	53	28 to 79	41 to 64
Both	230 singles 41 repeaters	271	58	16 to 84	45 to 71

[a] "Repeaters" are subjects treated twice, once by irradiation to the upper or lower body, and again sometime later to the other region.

[b] The "75% brackets" are the age limits centred on the mean within which three-quarters of the subjects fall.

TABLE II

Distribution of the 312 Cases by Site, Dose, and Sex

Site	Sex	Dose (rad) ≤600	Dose (rad) ca. 800	Dose (rad) ≥1000	Σ
Upper body	M	33	43	1	77
	F	17	43	0	60
	Both	50	86	1	137
Lower body	M	13	54	22	89
	F	7	29	50	86
	Both	20	83	72	175
Σ	M	46	97	23	166
	F	24	72	50	146
	Both	70	169	73	312

TABLE III

Distribution of the 312 Cases by Site, Dose, and Treatment

Site	Treatment of Cases	Dose (rad)			Σ
		≤600	ca. 800	≥1000	
Upper body	Singles	39	57	0	96
	Repeaters	11	29	1	41
	Both	50	86	1	137
Lower body	Singles	13	60	61	134
	Repeaters	7	23	11	41
	Both	20	83	72	175
Σ	Singles	52	117	61	230
	Repeaters	18	52	12	82
	Both	70	169	73	312

RESULTS

The first and most obvious thing to look at is, simply, whether or not the irradiation treatment was associated with vomiting by the patient. Before doing so, however, we must draw attention to one very relevant subgrouping, namely, whether the radiation field was truncated or not. In some instances the head was excluded from the upper-body field, and in some the feet were excluded from the lower-body field; this was done for clinical reasons such as absence of pain in these extremities. So we have four sites: U(e), U(t), L(e), and L(t), where U and L denote upper and lower body, and e and t stand for "entire" and "truncated".

The percentages of cases in which vomiting occurred (reactors) are given for the various groups in Table IV. Clearly the incidence of vomiting was higher in those receiving irradiation to the upper half of the body (81 per cent versus 44). There was no sex difference apparent among the U's but there was a greater percentage who vomited among the females in the L groups.

Sex	Body Region	
	U	L
M	78	29
F	85	59

This difference in response of men and women in respect of the two body regions is highly significant in statistical terms but its clinical significance is probably not great, especially since the pre- or post-menopausal status of the women was not investigated.

The probability of vomiting increased slightly with dose over the range studied, but in those subjects receiving radiation to the upper half of the body it was already 78 per cent in the lowest-dose group. An important point is that vomiting is not an inevitable consequence of irradiation; 15 of 86 patients receiving 800 rad to the upper half did not vomit.

A reactor we define as a case in which vomiting occurred following irradiation. Typically, a reactor would have a series of vomiting episodes separated by intervals. In theory several significant data from such records could be studied and analysed. In practice the choice is limited by a certain lack of resolution in the records - the timing of the onset and finish of an episode of vomiting is difficult and to some extent subjective. The nurses were not given special instruction on this matter. It might have been useful to introduce another observation, say, number of contractions, that would have helped give greater specificity in measuring vomiting duration.

After examining several possibilities during the analysis we decided to concentrate on two parameters: time to first episode (latency period), and time to last. However, before reporting these we shall look briefly at two other parameters: the number of episodes experienced by the reactors and the length of these. The observations on the former are summarized in Table V. The range is very wide, from 1 to 20 episodes per

TABLE IV

Percentage of Cases who Vomited (Reactors) by Site, Sex, and Dose

(Size of each group shown in brackets)

Site	Sex	Dose in rads			
		≤600	ca. 800	≥1000	All
U(e)	M	75% (16)	67% (15)	100% (1)	72% (32)
	F	86% (7)	91% (23)	- -	90% (30)
U(t)	M	88% (17)	79% (28)	- -	82% (45)
	F	60% (10)	90% (20)	- -	80% (30)
All U		78% (50)	83% (86)	100% (1)	81% (137)
L(e)	M	14% (7)	13% (15)	14% (7)	14% (29)
	F	33% (3)	40% (5)	50% (6)	43% (14)
L(t)	M	17% (6)	41% (39)	33% (15)	37% (60)
	F	100% (4)	50% (24)	66% (44)	63% (72)
All L		35% (20)	39% (83)	53% (72)	44% (175)

N.B. i) U and L denote upper and lower body respectively. The qualifier e means "entire", and t means "truncated"; see text.

ii) Because of the imbalance of the dose groups, the overall dose for the U's is somewhat smaller than that for the L's; consequently, the exhibited differences between the U and L vomitings are, if anything, underestimates.

iii) The pooling of the "singles" and repeaters" has its justification in the observation that, overall, the former included 60% reactors, and the latter 62%, i.e., they are indistinguishable.

TABLE V

Average Number of Episodes of Vomiting per Reactor, by Site, Sex, and Dose
(188 Reactors; the Range of Numbers of Episodes is 1 to 20)

(Size of each reactor group shown in brackets)

Site	Sex	Dose (rads)		
		⩽600	ca. 800	⩾1000
U(e)	M	4.0 (12)	5.3 (10)	2.0 (1)
	F	3.5 (6)	5.8 (21)	- -
	both	3.8 (18)	5.6 (31)	2.0 (1)
U(t)	M	4.5 (15)	5.1 (22)	- -
	F	2.5 (6)	6.8 (18)	- -
	both	3.9 (21)	5.9 (40)	- -
All U	M	4.3 (27)	5.2 (32)	2.0 (1)
	F	3.0 (12)	6.2 (39)	- -
	both	3.9 (39)	5.7 (71)	2.0 (1)
L(e)	M	4.0 (1)	1.0 (2)	4.0 (1)
	F	2.0 (1)	3.5 (2)	5.3 (3)
	both	3.0 (2)	2.3 (4)	5.0 (4)
L(t)	M	3.0 (1)	2.5 (16)	3.2 (5)
	F	2.5 (4)	3.7 (12)	4.1 (29)
	both	2.6 (5)	3.0 (28)	4.0 (34)
All L	M	3.5 (2)	2.3 (18)	3.3 (6)
	F	2.4 (5)	3.6 (14)	4.3 (32)
	both	2.7 (7)	2.9 (32)	4.1 (38)
All U & L	M	4.2 (29)	4.1 (50)	3.1 (7)
	F	2.8 (17)	5.5 (53)	4.3 (32)
	both	3.7 (46)	4.9 (103)	4.1 (39)

reactor. The overall average is 4.4 episodes and there are more in patients receiving 800 than in those receiving 600 rad. There does not seem to be any pattern which links the number of episodes with sex or irradiation area. We do not place much confidence in the usefulness of this aspect of the data because of the limitations of the reporting.

The other parameter we wish to discuss briefly is the duration of the individual episodes (which range in number from zero to 20 per case). Practical considerations in the hospital, plus the obvious difficulty of pinpointing the start and the finish of an episode, militated against the collection of hard data, but enough was acquired from 84 patients to give a rough picture - at least for upper-body irradiation at the 600 and 800 rad levels. The overall average of over 300 observations was just over 2 minutes, with the following breakdown:

	≤ 600 rad		ca. 800 rad	
Singles	[27]	2.05 (99)	[30]	2.53 (44)
Repeaters	[9]	1.85 (33)	[18]	2.34 (116)
Both		2.00 (132)		2.44 (260)

the main entries being minutes, the square bracketed figures numbers of patients, and the bracketed figures numbers of observations. There is no real difference between the "singles" and the "repeaters", but the higher dose cases commonly had slightly longer episodes (the difference 2.44 - 2.00 = 0.44, has a standard error of 0.11). So we see that the step from 600 to 800 rads is enough to induce longer episodes of vomiting as well as more episodes (see Table V). There is some evidence that the later episodes are a little shorter than the earlier ones which is to be expected. Incidentally, almost all episodes fell into the 1 to 5 minute range, but there were three records of 10-minute episodes and one of 20, and these "outliers" are probably hasty guesstimates (otherwise there would almost certainly be records of episodes that lasted between 5 and 10 and between 10 and 20 minutes).

The observations on the two key time parameters referred to above have been condensed into Table VI and VII. The coverage is of the 188 reactors and includes the "repeater" cases. It has been ascertained that there is no real difference, in this respect, between "singles" and "repeaters", so they need not be considered separately. For the same sort of reasons we have not distinguished between the sexes here, as a statistical analysis shows that they do not differ significantly in regard to the time intervals being studied. Thus we have twelve subgroups only - four sites at each of three dose levels. Both the means and the medians are shown so that some idea of the distribution of the times can be gathered.

From Table VI we see that the time to the first episode (the latency period) is generally shorter among the U-treated reactors than among the L-treated. At 800 rad the mean latency period in the U's is less than an hour; and in the L's it is almost two hours. The overall means are 57 minutes for the U groups and 98 for the L groups, a difference of

TABLE VI

Interval (minutes) from Start of Irradiation to First Episode (the 188 reactors only)

Site	Dose (rad)								
	≤600			ca. 800			≥1000		
	Mean	Med'n	(No.)	Mean	Med'n	(No.)	Mean	Med'n	(No.)
U(e)	65	59	(18)	51	46	(31)	154	154	(1)
U(t)	69	67	(21)	49	45	(40)	-	-	-
L(e)	78	78	(2)	124	97	(4)	60	60	(4)
L(t)	80	50	(5)	109	90	(28)	94	74	(34)

N.B.: "med'n" is the median value, i.e., the middle value when the intervals are arranged in order of magnitude.

TABLE VII

Interval (minutes) from Start of Irradiation to Last Episode (the 188 reactors only)

Site	Dose (rad)								
	<600			ca. 800			>1000		
	Mean	Med'n	(No.)	Mean	Med'n	(No.)	Mean	Med'n	(No.)
U(e)	142	154	(18)	154	152	(31)	239	239	(1)
U(t)	156	163	(21)	147	145	(40)	-	-	-
L(e)	158	158	(2)	171	191	(4)	229	212	(4)
L(t)	148	147	(5)	169	169	(28)	184	186	(34)

TABLE VIII

Mean Interval (minutes) from the First to the Last Episode - i.e., the duration of emesis. Only those groups with more than five cases are included. The size of each group is given in brackets.

	Dose (rad)		
Site	≤600	ca. 800	≥1000
U(e)	77 (18)	103 (31)	-
U(t)	87 (21)	98 (40)	-
L(e)	-	-	-
L(t)	-	60 (28)	90 (34)

TABLE IX

Percentage	Time (min) at which Percentage is Reached of Persons Exposed		of Persons who Vomit	
	Start	Stop	Start	Stop
10	18	47	16	42
30	41	108	34	89
50	76	201	57	151
70	166	440	96	255
90	-	-	205	544

N.B.: Based on 137 exposed persons who received radiation to the upper half of the body. In the group there were 111 who vomited. For the cumulation percentages the distribution assumed is lognormal.

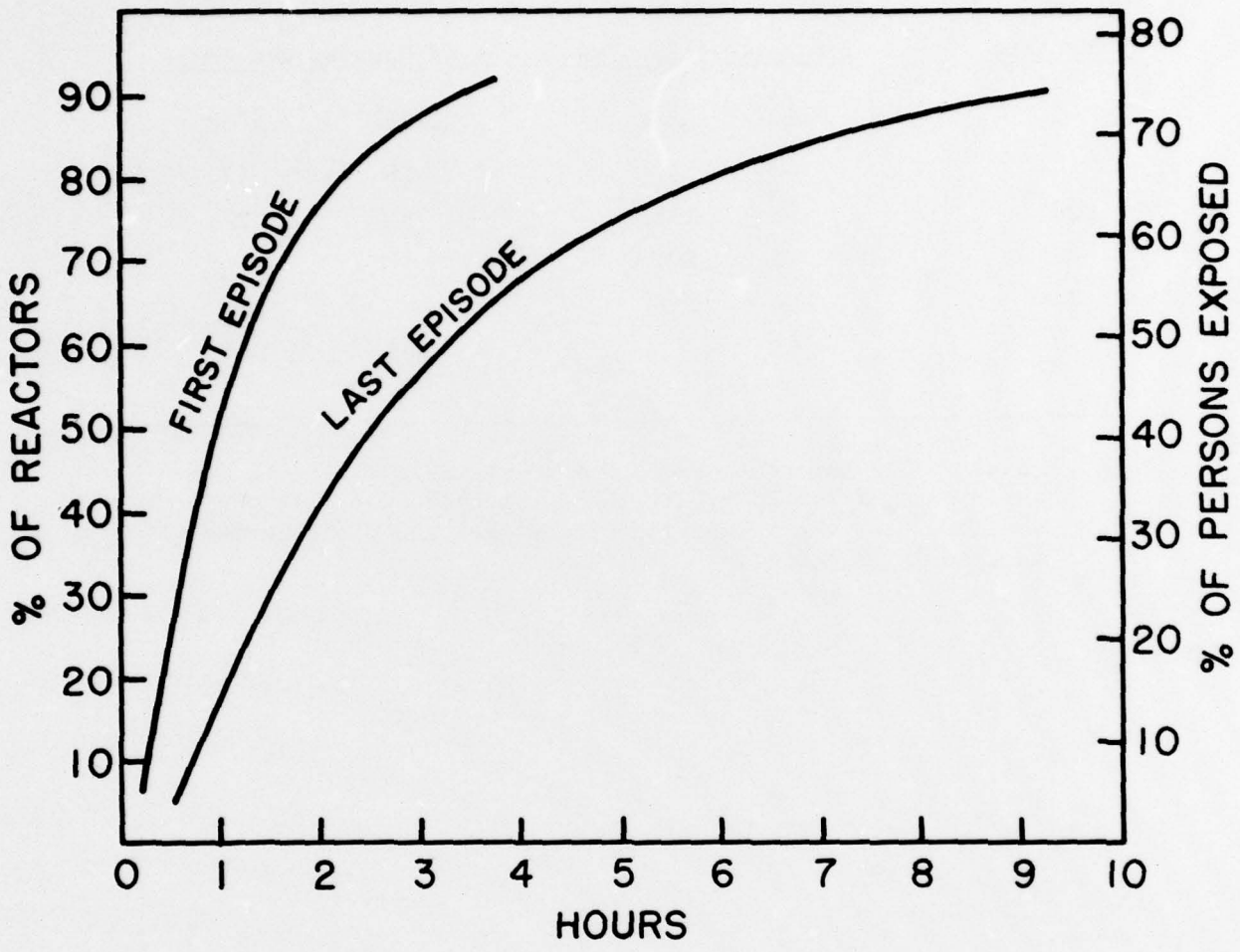

Fig. 2. As a function of time after the start of irradiation, the percentage of those exposed (right-hand axis) and the percentage of those who vomit (left-hand axis) who have their first or last episode. This information is also available in Table IX.

41 minutes, which is considerable. Table VII gives, equivalently, times from the start of irradiation to the final episode. (In those cases in which there was only one episode, its time was taken as the final.) Here again the times are shorter in the U groups than in the L groups, the overall means being 151 and 177 respectively, although the difference, 26 minutes, is less than that for the latency periods.

The variable time required to turn the patient contributed most prominently to the differences in the total time necessary to deliver the stated dose. Because of these differences, the latency periods were determined using the beginning of irradiation as the operational time zero. Close analysis of the data indicates that it is not strictly acceptable, in all cases, to merely subtract the overall mean duration of irradiation (30 ± 13.5 SEM) to determine the latency periods relative to the end of irradiation. However, this average figure is included for the information of the reader.

Table VIII derives from Tables VI and VII; it gives the mean interval from the first to the last episode, that is the duration of emesis, and concentrates on the six groups (three pairs of groups, at approximately 200 rad dose intervals) that are big enough to furnish estimates of the differences in times over the dose range. Specifically, we see that the mean duration of emesis increases with dose, as is to be expected. From the three Tables (VI, VII and VIII) we can calculate the following mean increases in time per extra 100 rad dosage:

To first episode	-	-8 minutes
Duration of emesis	-	11 minutes
To last episode	-	3 minutes

which are of course consonant. The gradations are fairly small. It would be improper to assume that they are applicable to doses outside the observed range, 600 to 1000, for the linearity on which our estimates are based cannot extend very far.

Court Brown and Abbatt (1954) claimed there was a reciprocal correlation between the latency period and the duration. We searched for such a relationship in our data, but it was not present. This means that the time to the first episode of vomiting is not a good indicator of the duration of the vomiting period.

We have also analysed a subset of the data to provide estimates of the percentages of a population with the upper-half exposed to radiation that vomit or recover (cease to vomit) at various times (Fig. 2 and Table IX). These estimates are based on the reasonable assumption of a log-normal distribution of recovery times - at one end of the spectrum there also are subjects who recover quickly, and at the other end there are those who suffer longer (some of whom may even die and thus have an effective recovery time of infinity). It would be unwise to press this extrapolative analysis very far, but at least it gives the order of onset and recovery times that may be expected in a sizable group, which will be of value in a military context.

DISCUSSION

It is very difficult to make precise statements about the response of human subjects in good health to radiation because such a situation would only occur accidentally or in a nuclear war. The first is extremely rare, and nuclear weapons have been used against human populations only at Hiroshima and Nagasaki. There were neither adequate observations nor dosimetry in Japan, and therefore very little precise information about the early medical history of those exposed. Because of the deficiencies it has been necessary to place heavy reliance on data collected from cancer patients in predicting human response to radiation.

For military purposes the greatest interest perhaps lies in life-threatening whole-body doses, and few patients receive such treatment. Another consideration is that soldiers, in contrast to patients, would be called on to perform demanding duties post-exposure without major medical support. The patients who receive treatments of greatest military interest are generally receiving palliative care and are close to death because of their condition. Nausea and vomiting, let alone anorexia and fatigue, are very frequently side-effects of their condition even before they are irradiated. One must bear these caveats in mind when basing predictions on the observations in the literature and those reported here.

The data set included in this report is derived from a large group of cancer patients who received doses of radiation to either the upper or lower half of their bodies. They were all seriously ill, but many were not confined to bed; they were not called upon to perform any task post-exposure. A comparison of data gathered from upper- or lower-body irradiations shows that upper-body irradiation resulted in a reduction in the latent period before the onset of vomiting and a larger percentage of patients vomiting. In the case of those who received 800 rad to the upper half the mean times to the first and last vomiting episodes were 50 and 150 minutes respectively. Some patients did not vomit after 800 rad to the upper half-body.

The uniqueness of this study lies mainly in the precise information on timing of emesis obtained with a large number of patients. Previous reports have concentrated on the dose-dependence of the response rather

than its timing. Our results confirm and extend those of Rider and Hasselback (1968) who found that the latent period was 45 to 60 min and the total duration up to 6 hours. The latent period before vomiting occurred was longer in the studies reported by Court Brown and his colleagues, but the radiation they used was not so penetrating and was concentrated in the area of the pelvis and spinal cord. Gerstner (1960) likewise found the latent period was 3 hours. Since the sensitive target in the body is not known one cannot compare these studies further.

A further point is that the length of each vomiting episode is short and their number is small (Table V). Although our study does not address this question directly, the clinical impression formed was that discomfort and nausea were much greater at the time of vomiting than in the intervening periods. The notes by the nurses indicate that many patients slept between episodes. It seems unlikely that personnel in combat would experience as much nausea as assumed by Brookman and Hoffman (1977) in developing their very interesting scenario of the impact of nausea and vomiting on the outcome of a tank battle.

After the main body of the work was completed two patients were irradiated at dose rates less than 5.0 rad/min to examine the possibility that emesis would be less prevalent. Both vomited several times, starting about 1 hour after the radiation commenced (dose received at that time about 300 rad). More details are given in Appendix 2. This finding, together with reports by Lushbaugh et al. (1968), indicate that fallout as well as prompt radiation may cause emesis.

The difference in sensitivity between whole-body and upper half-body radiation in terms of production of emesis is not known, but it is unlikely that they would be very different. Further, there is no evidence from this study of a marked dose-dependence. One can therefore take the times shown in Fig. 2 and Table IX for the times at which various percentages of the population would vomit as a reasonable prediction for a military group exposed to whole-body radiation in excess of 200 rad; any error is likely to be in the direction of over-estimating the speed of onset. According to Table IX, 50 per cent of those exposed would have commenced vomiting at 76 min and would have had their last episode by 201 min. Estimates of times for other percentages of those exposed, and on the alternative basis - those who responded by vomiting rather than the whole group exposed - can be obtained from Table IX.

Little is known about the fatigue which is reported by irradiated persons. The effect of fatigue on performance would be affected greatly by motivation, and this is one of the many complications which confound attempts to predict performance of irradiated personnel. Payne (1959), who studied some of the patients irradiated by Miller et al. (1958), could detect no effect of 200 r (130 rad absorbed dose) on the performance of various tests of psychomotor skills used for testing pilot-recruits. Payne studied the patients at daily intervals starting 1 hour after irradiation, and surprisingly made no mention of the prodromal effects reported by Miller et al. It is not clear whether they were experiencing symptoms such as nausea and vomiting while being tested. Fatigue would be a very important factor in determining the effectiveness of military personnel and it should not be assumed that

they would be fully fit for combat duty when the vomiting had ceased. The longer recovery times from the prodromal syndrome given in STANAG 2866 should be followed to allow time for complete recovery from other aspects of the syndrome such as fatigue (see Fig. 1).

ACKNOWLEDGMENTS

We are indebted to Drs. C.E. Danjoux, C.J.H. Fryer, M. Holecek, and T. Keane, and Mrs. S.G. Fowler, RN, of the Princess Margaret Hospital for their assistance. Mr. P. Clay and Mrs. L. Bramall of the Biomathematics Group at the National Research Council and Mrs. E. Inhaber of DREO collaborated with us in the data processing.

REFERENCES

1. P.J. Fitzpatrick and W.D. Rider, Half body radiotherapy. Int. J. Radiation Oncology Biol. Phys. 1, 197-207 (1976).

2. STANAG 2866 (NBC/MED) - Medical effects of ionizing radiation on personnel, Military Agency for Standardization, North Atlantic Treaty Organization.

3. T. Ohkita, A review of thirty years study of Hiroshima and Nagasaki atomic bomb survivors II Biological effects A. Acute effects Supplement to J. Radiation Res. 49-66 (1975).

4. W.M. Court Brown and R.F. Mahler, Discussion on the radiation syndrome. Proc. Roy. Soc. Med. 46, 245-250 (1953).

5. L.S. Miller, G.H. Fletcher and H.B. Gerstner, Radiobiologic observations on cancer patients treated with whole-body X-irradiation. Rad. Res. 8, 150-165 (1958).

6. W.M. Court Brown and J.D. Abbatt, Observations made on the human response to a single dose of X-rays - the latent period in Radiobiology Symposium, Liege edited by Z.M. Bacq and P. Alexander, 229-234 (1954).

7. H.B. Gerstner, Reaction to short-term radiation in man. Ann. Rev. Med. 11, 289-302 (1960).

8. C.C. Lushbaugh, F. Comas and R. Hofstra, Clinical studies of radiation effects in man. A preliminary report of a retrospective search for dose-relationships in the prodromal syndrome. Radiation Res. Suppl. 7, 398-412 (1967).

9. W.H. Langham, Radiobiological factors in manned space flight: Report of the Space Radiation Study Panel of the Life Sciences Committee, Publication 1487. National Academy of Sciences/National Research Council, Washington, D.C., pp. 76-90 (1967).

10. C.C. Lushbaugh, F. Comas, C. Lowell Edwards and G.A. Andrews, Clinical evidence of dose-rate effects in total-body irradiation in man, in Dose Rate in Mammalian Radiation Biology edited by D.G. Brown, R.G. Cragle and T.R. Noonan for UT-AEC Agricultural Research Laboratory and USAEC (Conf. - 680410) (1968).

11. W.D. Rider and R. Hasselback, The symptomatic and haematological disturbance following total body radiation of 300-rad gamma-ray irradiation in Guidelines to Radiological Health, Public Health Service Publication No. 999-RH-33, U.S. Department of Health, Education and Welfare, pp. 139-144 (1968).

12. M.A. Brookman and M.L. Hoffman, Methodologies for evaluating the impact of time-variable nuclear effects on small-unit combat operations. Defense Nuclear Agency, Washington, DC 20305, DNA 4318F (AD-A0521291) (1977).

13. R.B. Payne, Effects of ionizing radiation on human psychomotor skills. U.S. Armed Forces Med. J. 10, 1009-1021 (1959).

APPENDIX I

DATA TREATMENT AND ANALYSIS

Figure 1 (a and b) is a copy of the data sheet which was completed by the radiotherapist and attending nurse. The data were taken from these sheets and coded onto punch cards.

To facilitate future analysis and recall, an effort was made to code a maximum amount of information. This decision was made only after completion of the data collection. Each "event" was coded in the order of its occurrence. Events included: food taken up to 2 hours before irradiation, including information on whether it was solid or liquid; starting time of irradiation; starting time and duration of each vomiting episode; time of other effects which were classed as detrimental, such as cramps or diarrhoea; quantity of liquid, solid or intravenous intake after irradiation.

Particular attention was paid to the drugs prescribed for each patient. A total of 26 drugs were prescribed. Some patients received no drug therapy, however, many received more than one. The majority of the drugs prescribed were analgesics. In each case the time of drug introduction was noted and whether it was premedication, taken up to two hours before irradiation, or medication, received after irradiation. The quantity and route of administration were also listed for each dose.

Four drugs with reputed anti-nausea or anti-vomiting actions were prescribed. Chlorpromazine (Largactil) and dimenhydrinate (Gravol) were employed a few times without apparent beneficial affect. Prochlorperazine (Stemetil) and metoclopramide (Maxeran) were also prescribed. These drugs were prescribed on the basis of need. For instance, an individual who complained of significant vomiting at his first treatment would possibly receive Stemetil or Maxeran prior to a second half-body irradiation. The drugs were also administered to patients during bouts of difficult vomiting. Since these drugs were not distributed blind or on a random basis, and since they were often present in concert with other medications, it is not possible to make clear statements concerning their effectiveness. The majority of patients did not receive any anti-nausea or anti-vomiting medication. It was the clinical judgment of the attending physicians that these medications were of little value.

As mentioned in the main results section of this report, recorded data on the incidence of nausea was ignored. This was done mainly because nausea records did not appear to be independent. The vomiting qualifiers A-C were recorded and were given equal weighting in the analysis. It was reasoned that the amount vomited would depend on incidence of recent vomiting episodes and on food consumption. It was also assumed that retching was

equally as disruptive as vomiting. An attempt was made to code other qualifiers to learn more about attending symptoms and the source of vomitus. Yellow-green staining was taken to imply reflux of intestinal contents into the stomach, while black to red staining implicated various stages of gastric bleeding. Since the forms did not ask for this information, the records are incomplete.

We have not been successful in making use of much of the data we have recorded but have retained the punched cards for possible future use.

Fig. 1a

Hospital: _____ Date: _____

Radiotherapist in Charge: _____

Data Collection by: _____

Patient code No. _____

Sex _____ Age _____ Weight _____ Height _____

Other relevant measurements _____

_____

Therapy Data

Physics Radiation quality _____ Energy _____

(equipment and method, e.g. rotation, static, etc.)[1]

Dose rate _____

Total dose[2] _____

Anatomical area exposed _____

Posture during irradiation _____

Dosimetry - calculation _____

physical measurement _____

Medical Data

Current medication _____

Disease and state _____

_____

Observed Response Data

Time of onset of vomiting (from start of irradiation)[3,4] _____

Duration _____

Frequency _____

Notes:
1. Information to be forwarded to include such data as to whether the patient had a single exposure, a bilateral exposure, or whether the course or patient was rotated during exposure.
2. Total dose to be given in terms of surface (skin) dose (rads), midline exposure in air or midline tissue dose (rads).
3. In the case of bilateral irradiation the time of commencement of irradiation of each side and time interval between is to be noted.
4. All observations to the nearest fifteen minutes during the first 24 hours.

Fig. 1b

PRINCESS MARGARET HOSPITAL

DEPARTMENT OF NURSING

FOOD OR FLUIDS TAKEN DURING 2 HOUR PERIOD PRECEDING IRRADIATION	
Approx. Time	Type of Nourishment

Pre-treatment assessment - Nursing

CURRENT MEDICATIONS

PREMEDICATION	
Time Given	

DATE	NAUSEA 1 Pt. feels 'squeamish' 2 Pt. would like to vomit 3 Pt. is going to vomit	VOMITING A More than 100 ml. B Less than 100 ml. C Retching-no vomiting

TIME	NAUSEA 1	2	3	VOMITING A	B	C	Comments, Medications, etc.
							Irradiation started
							Turnover
							Irradiation finished
							DATA SHEETS ADDED AS NEEDED

APPENDIX II

LOW DOSE-RATE

Two patients, both middle-aged males (aged 41 and 48), have recently been irradiated. They received 4.82 or 4.90 rads/min whole-body radiation, total mid-plane dose 1000 rads, from an overhead 1.25-MeV ^{60}Co source. They received the first half of the dose in the supine position. Immediately following turnover they received the second 500 rads.

Both patients vomited at approximately one hour after the beginning of irradiation, total accumulated dose 225 and 335 rads. Further vomiting information is seen in Table I. It is noteworthy that vomiting did occur and that the latent period, prior to the first vomiting episode, is similar to that seen in the higher-dose-rate, half-body irradiations.

The low-dose-rate radiotherapy program was initiated by the radiotherapist following suggestions that this procedure results in a lower incidence of vomiting. Since no ameliorating effect has thus far been seen it is likely that few, if any, patients will be added to the study. The present results are reported to provide some indication of a possible lack of dose-rate dependence. However, the sample size is clearly too small to allow for many conclusions beyond the fact that vomiting may occur and a latent period of one hour may be a reasonable estimate.

It should be noted that the two patients received their 1000 rads as part of a bone marrow replacement program. Patient 1 had acute myeloid leukemia and patient 2 had acute leukemia. Both received significant doses of the cytotoxin cyclophosphamide (aimed at destroying cancerous bone marrow) and antibiotics (to "sterilize" the gut and reduce subsequent infection). These drugs were not given on the day of irradiation. Patient 1 received a 20-mg oral dose of diazepam (Valium) 30 min before irradiation. He was also maintained on an intravenous saline drip during the 4.5-hour irradiation period which also delivered a total of 30 mg metoclopramide (Maxeran). Patient 2 was less alert. He was heavily sedated with a continuous intravenous infusion of diazepam (Valium), delivering 22-mg in a 6-hour period beginning at the onset of radiation.

TABLE I

Vomiting Following Low-Dose-Rate Irradiation

Patient	Dose Rate rad/min	Vomiting Episodes		
		#	Time from start of irradiation (min)	Total accumulated dose (rad)
1	4.90	1	68	335
		2	100	400
		3	130	460
		4	145	510
		5	160	570
		6	180	640
		7	195	700
		8	205	760
2	4.82	1	57	225*
		2	145	550
		3	230	900

* Expected dose at 57 min = 275 rad. 10-min. shut-down accounts for discrepancy.

Each vomiting episode and the turnover at 500 rad required a further shut-down.

Unclassified

Security Classification

DOCUMENT CONTROL DATA - R & D

(Security classification of title, body of abstract and indexing annotation must be entered when the overall document is classified)

1. ORIGINATING ACTIVITY
Defence Research Establishment Ottawa
Department of National Defence
Ottawa, Ontario, Canada K1A 0Z4

2a. DOCUMENT SECURITY CLASSIFICATION

2b. GROUP

3. DOCUMENT TITLE
A PREDICTIVE STUDY OF THE INCIDENCE OF VOMITING IN IRRADIATED MILITARY PERSONNEL

4. DESCRIPTIVE NOTES (Type of report and inclusive dates)
Project Report 1974 - 1978

5. AUTHOR(S) (Last name, first name, middle initial)
Grant, George A., Cairnie, Alan, B., Harding, R. Kent, Gridgeman, Norman T., Rider, Walter, D.

6. DOCUMENT DATE	7a. TOTAL NO. OF PAGES	7b. NO. OF REFS
November 1979	31	13

8a. PROJECT OR GRANT NO.	9a. ORIGINATOR'S DOCUMENT NUMBER(S)
	DREO Report No. 817
8b. CONTRACT NO.	9b. OTHER DOCUMENT NO.(S) (Any other numbers that may be assigned this document)

10. DISTRIBUTION STATEMENT

11. SUPPLEMENTARY NOTES	12. SPONSORING ACTIVITY
	Radiation Biology Section Protective Sciences Division, DREO

13. ABSTRACT

The scientific literature on the incidence in man of vomiting and other prodromal effects of ionising radiation is analysed and related to the guidance given in STANAG 2866. New data obtained from observations of 271 patients who received 600 to 1000 rad to either the upper or lower half of the body are analysed. The incidence of vomiting was 81 per cent in those who received radiation to the upper half of the body and 44 per cent for the lower half. The time to the first and last vomiting episodes for upper-body radiation were on average about 60 and 150 min from the start of the irradiation. The average number of episodes was 4.5; the average duration of an episode just over 2 min. None of these parameters changed appreciably with the doses used. Predictions are made of the time required for various percentages of military personnel to start, and then to finish, vomiting after being exposed to radiation.

DSIS
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KEY WORDS

Prodromal Symptoms
Radiation-Induced-Vomiting
Radiation Effects
Human Performance

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